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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/508,418	06/08/2000	MAMORU HORIKOSHI	Q58140	1158

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	28

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/508,418	HORIKOSHI ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *10 February 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attachment*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: *2 and 5*.

Claim(s) rejected: *1 and 8*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *Notice of Reference Cited, Form PTO-892*

ADVISORY ACTION

[1] Claims 1, 2, 5, and 8 are pending in the application.

[2] Claims 1 and 8 stand finally rejected.

[3] Claims 2 and 5 are objected to as being dependent upon a rejected claim but are otherwise in condition for allowance.

[4] Applicant's amendment to claims 1, 2, and 8 and cancellation of claims 9-26 in Paper No. 26, filed July 01, 2003, is acknowledged.

[5] The request for reconsideration is acknowledged, however the amendment does not place the application in condition for allowance for the reasons stated below.

[6] It is noted that applicant's arguments addressing rejections under 35 USC 112, second paragraph (items IA and IB at page 4 of Paper No. 26) and a rejection under 35 USC 112, first paragraph (item IC at page 5 of Paper No. 26) are directed to rejections that have been previously withdrawn in view of applicant's amendment of Paper No. 24 (see item 7 of Paper No. 25). Also, applicant's arguments addressing rejections under 35 USC 112, first paragraph (items ID and IE at pages 5-7 of Paper No. 26) and rejections under 35 USC 102(b) and 102(e) (items IIA and IIB at pages 7-9 of Paper No. 26) are directed in part to claims that have been canceled and applicants arguments have been addressed to the extent that the rejections apply to pending claims.

[7] The written description rejection of claims 1 and 8 under 35 USC 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in previous Office actions (see item 11 of Paper No. 13, item 6 of Paper No. 21, and item 8 of Paper No. 25). Applicant argues (part ID at pages 5-6 of Paper No. 26) claim 1 has been amended to recite specific pyrazole compounds and amended claim 1 recites the organism from which the protein is isolated. Applicant argues the amended claims encompass only those proteins derived from one organism, having a specific activity, and having resistance to a specific group of chemical compounds, and mutants thereof. Applicant argues the amendment limits the claims to a very small group of proteins that have adequate written description. Applicant argues a discussion of the types of mutations that may be made to the

mutant peptide is found in the specification. Applicant's argument is not found persuasive. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a "representative number of species" means that the species that are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the genus of claimed polypeptides, i.e., the polypeptide of SEQ ID NO:2. The specification fails to describe the structures of any additional representative species of the claimed genus. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the claimed genus of polypeptides encompasses species that are widely variant in structure and read on *any* protox polypeptide having the activity as set forth in claim 1. Contrary to applicant's assertion that the polypeptide is limited to a protein derived from a single organism, the claimed mutant polypeptide is not limited to a protox from *N. tabacum* and can be from any source and have any structure. As such, the disclosure of the single representative species of SEQ ID NO:2 is insufficient to be representative of the attributes and features of *all* species encompassed by the claimed genus of polypeptides. Given the lack of description of a representative number of polypeptides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[8] The scope of enablement rejection of claims 1 and 8 under 35 USC 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in previous Office actions (see item 12 of Paper No. 13, item 7 of Paper No. 21, and item 9 of Paper No. 25). Applicant argues (part IE at pages 6-7 of Paper No. 26) the scope of the claims encompasses only those polypeptides that are derived from one organism, having a specific activity, and having resistance to a specific group of chemical compounds, and mutants thereof. Applicant argues the specification teaches a skilled artisan how to make and use the entire scope of claimed polypeptides. Applicant argues in view of the narrow scope of the claims and the teachings of the specification, undue experimentation would not be required to make and use the entire scope of the claims. Applicant's argument is not found persuasive. It is noted that the claimed polypeptide is not limited to a polypeptide isolated from *N. tabacum*. Contrary to applicant's assertion that the polypeptide is limited to a protein derived from a single organism, the claimed mutant polypeptide is not limited to a protox from *N. tabacum* and can be from any source and have any structure. Thus, the polypeptide of claim 1 is so broad as to encompass *all* polypeptides having the recited activity. The specification provides only a single working example of the claimed polypeptide, i.e., SEQ ID NO:2 and fails to teach a skilled artisan how to make the entire scope of mutant protox polypeptides. The specification fails to provide guidance regarding those amino acids of SEQ ID NO:2 that may be altered by substitution, addition, or deletion with an expectation of maintaining the desired activity. Predictability of which changes can be tolerated in an encoded protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining an encoded polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single

mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). While it is acknowledged that this reference was published in 1991, to date there remains no certain method for reasonably predicting the effects of even a single amino acid mutation on a protein. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

[9] The rejection of claims 1 and 8 under 35 USC 102(b) as being anticipated by Ward et al. (WO 95/34659) is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in previous Office actions (see item 13 of Paper No. 13, item 8 of Paper No. 21, and item 10 of Paper No. 25). Applicant argues (part IIA at pages 7-8 of Paper No. 26) the polypeptide of Ward et al. is not isolated from *N. tabacum* and does not provide a 10-fold increase in herbicide resistance. Applicant's argument is not found persuasive. Contrary to applicant's assertion that the polypeptide is limited to a protein isolated from *N.* tabacum, the claimed mutant polypeptide is not limited to a protox from *N. tabacum* and instead can be a protox from any source and have any structure. It is noted that the polypeptide of claims 1 and 8 is not limited to a polypeptide that has a level of herbicide resistance to that of SEQ ID NO:2. Instead, the polypeptide is limited to an activity "equivalent to that of the polypeptide represented by SEQ ID NO:2, i.e., protox activity. The polypeptide of Ward et al. is disclosed as having protox activity. Therefore, the teachings of Ward et al. anticipate the claims as written.

[10] The rejection of claim 1 under 35 USC 102(e) as being anticipated by Volrath et al. (US Patent 5,939,602) is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in previous Office actions (see item 14 of Paper No. 13, item 9 of Paper No. 21, and item 11 of Paper No. 25). Applicant argues (part IIB at pages 8-9 of Paper No. 26) the polypeptide of Volrath et al. is distinct from the claimed polypeptide as the polypeptide of Volrath et al. does not have an enzyme

activity equivalent to SEQ ID NO:2 and does not anticipate the claim. It is noted that the polypeptide of claims 1 and 8 is not limited to a polypeptide that has a level of herbicide resistance to that of SEQ ID NO:2. Instead, the polypeptide is limited to an activity "equivalent to that of the polypeptide represented by SEQ ID NO:2, i.e., protox activity. The polypeptide of Volrath et al. is disclosed as having protox activity. Therefore, the teachings of Volrath et al. anticipate the claims as written.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:00 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for submission of official papers to Group 1600 is (703) 308-4242. Draft or informal FAX communications should be directed to (703) 746-5078. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman
Patent Examiner
Art Unit 1652

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GROUP ~~1800~~ 1600